

AMENDMENTS

Please enter the following amendments:

Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1.-3. (canceled)

4. (currently amended) A hybrid oligonucleotide ~~consisting of~~ comprising one or more deoxyribonucleotide POPS blocks, the POPS blocks comprising alternating phosphorothioate and phosphodiester internucleoside linkages, ~~and one or more~~ flanked by regions of at least two contiguous 2'-O-substituted ribonucleotides ribonucleosides, wherein the 2'-O-substituted ribonucleotides ribonucleosides are linked by internucleoside linkages selected from the group consisting of phosphodiester and phosphorothioate internucleoside linkages.

5. (currently amended) The hybrid oligonucleotide according to claim 4, having from 12 to 50 nucleotides.

6. (currently amended) The hybrid oligonucleotide according to claim 4, having from 17 to 35 nucleotides.

7. (previously presented) The hybrid oligonucleotide of claim 4, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of from 1:3 to 3:1.

8. (previously presented) The hybrid oligonucleotide of claim 7, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of about 1:1.

9. (previously presented) The hybrid oligonucleotide of claim 7, wherein the phosphorothioate and phosphodiester internucleoside linkages alternate in a manner selected from the group consisting of one-to-one, two-to-one, one-to-two, two-to-two and three-to-three.

10. **(currently amended)** The hybrid oligonucleotide of claim 4, wherein the ~~one or more~~ regions of 2'-O-substituted ~~ribonucleotides~~ ribonucleosides are linked by phosphodiester internucleoside linkages.

11. **(currently amended)** The hybrid oligonucleotide of claim 4, wherein the ~~one or more~~ regions of 2'-O-substituted ~~ribonucleotides~~ ribonucleosides are linked by phosphorothioate internucleoside linkages.

12. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-halogen selected from the group consisting of 2'-Cl, 2'-Br, and 2'-F.

13. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-lower alkyl group containing 1-6 saturated or unsaturated carbon atoms, wherein such alkyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more such chemical groups.

14. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-aryl or allyl group containing 2-6 carbon atoms, wherein such aryl or allyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more such chemical groups.

15. **(new)** An inverted hybrid oligonucleotide comprising one or more regions of 2'-O-substituted ribonucleosides linked by phosphodiester and/or phosphorothioate internucleoside linkages, wherein the one or more regions of 2'-O-substituted ribonucleosides are flanked by regions of deoxyribonucleoside POPS blocks, the POPS blocks comprising alternating phosphorothioate and phosphodiester linkages.

16. **(new)** The inverted hybrid oligonucleotide according to claim 15, having from 12 to 50 nucleotides.

17. **(new)** The inverted hybrid oligonucleotide according to claim 15, having from 17 to 35 nucleotides.

18. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of from 1:3 to 3:1.
19. **(new)** The inverted hybrid oligonucleotide of claim 18, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of about 1:1.
20. **(new)** The inverted hybrid oligonucleotide of claim 18, wherein the phosphorothioate and phosphodiester internucleoside linkages alternate in a manner selected from the group consisting of one-to-one, two-to-one, one-to-two, two-to-two and three-to-three.
21. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the one or more regions of 2'-O-substituted ribonucleosides are linked by phosphodiester internucleoside linkages.
22. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the one or more regions of 2'-O-substituted ribonucleosides are linked by phosphorothioate internucleoside linkages.
23. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-halogen selected from the group consisting of 2'-Cl, 2'-Br, and 2'-F.
24. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-lower alkyl group containing 1-6 saturated or unsaturated carbon atoms, wherein such alkyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more of such chemical groups.
25. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-aryl or allyl group containing 2-6 carbon atoms, wherein such aryl or allyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more of such chemical groups.